

Reproductive Physiology

Hypothalamic-Pituitary- Gonadal-Axis

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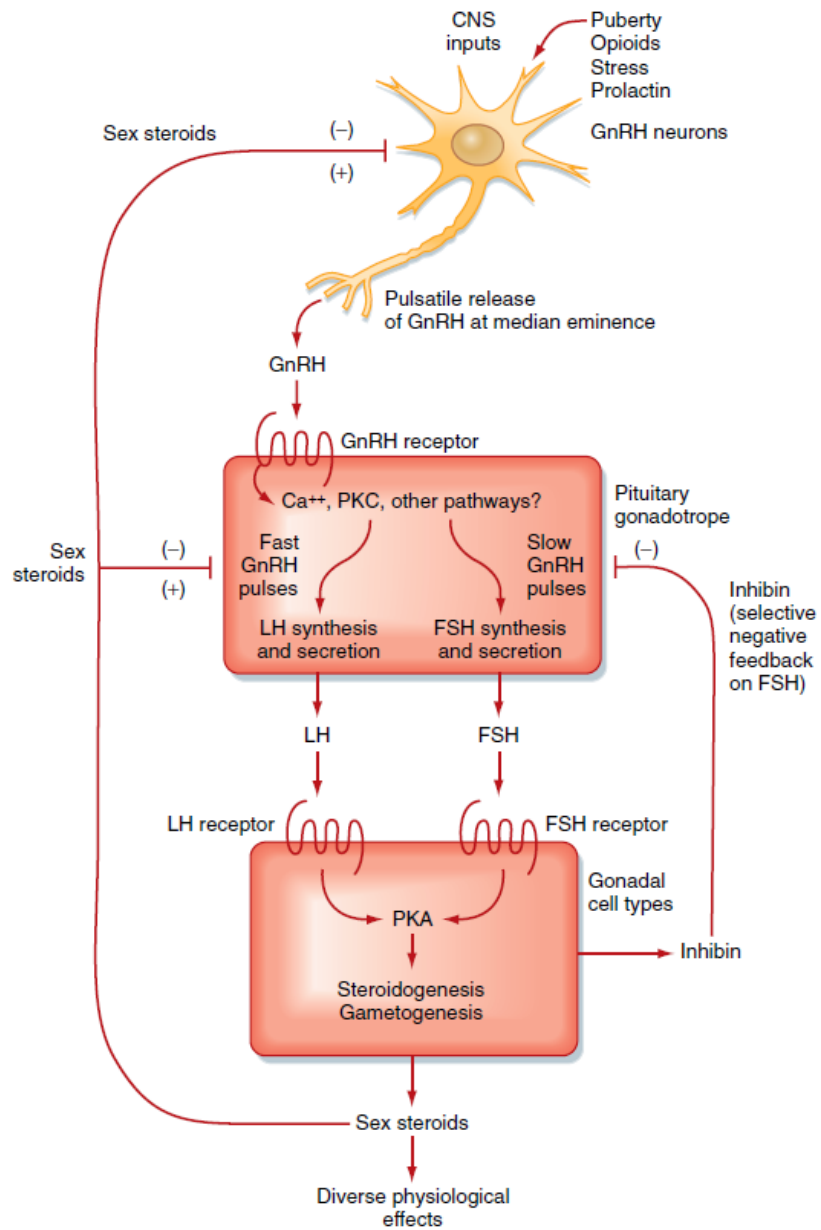
Objectives

By the end of this lecture, you should be able to:

1. Characterize hypothalamic pituitary relationship
2. Name the hypophysiotropic hormones and outline the effects that each has on anterior pituitary function
3. Name anterior pituitary gonadotropic hormones and outline the effects that each has on the gonads
4. Describe the negative and positive feedback mechanisms in the hypothalamic-pituitary-gonadal axis and their importance in the control of reproductive function

Keywords: GnRH, FSH, LH, androgens, estrogens

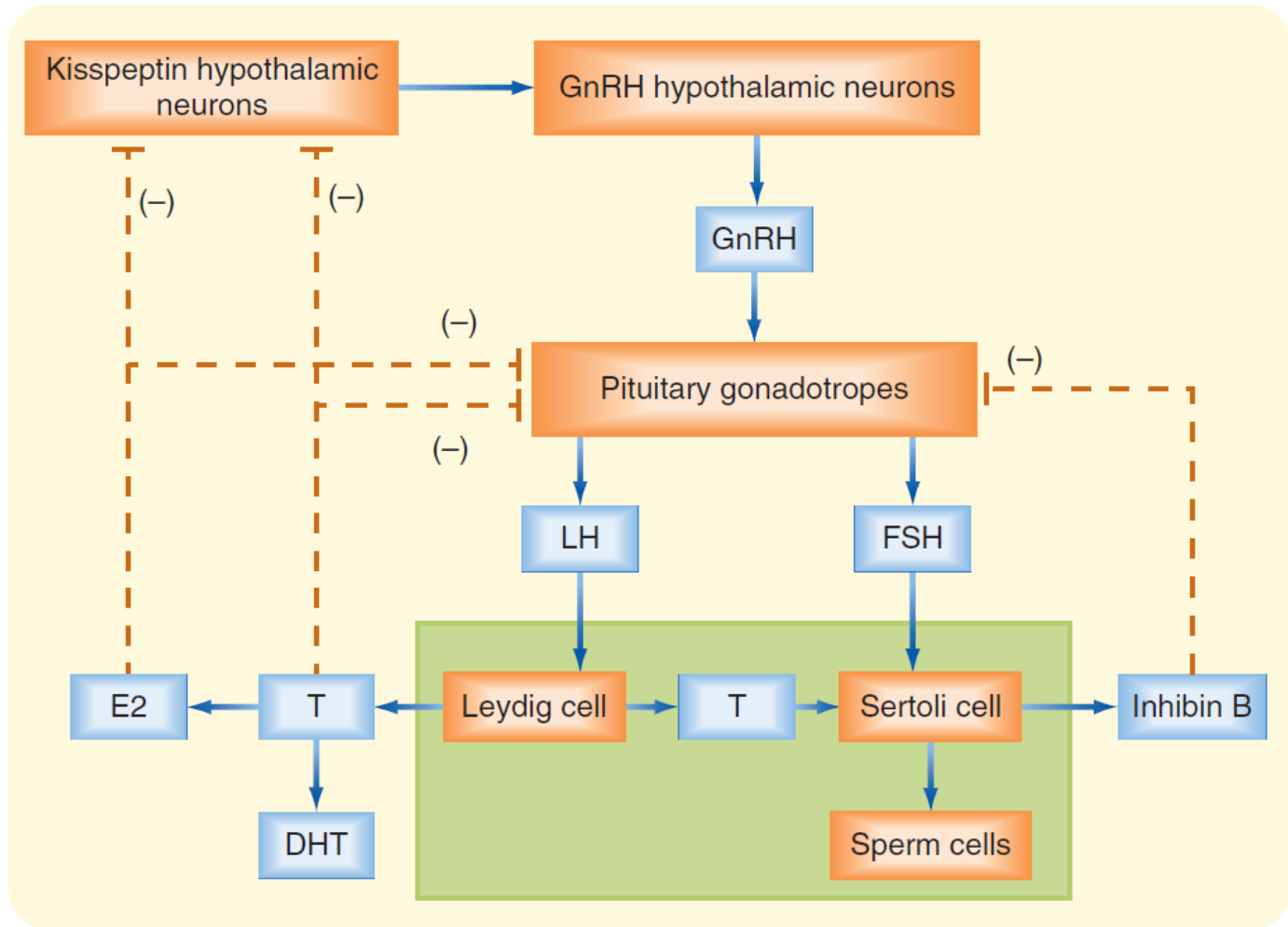
HPG



Regulation of Reproduction: General Pathways

- **Hypothalamus:**
 - Gonadotropin releasing H (GnRH)
- **Anterior Pituitary**
 - Lutenizing H (LH)
 - Follicle stimulating H (FSH)
- **Ovary:**
 - Estrogen, progesterone, Inhibin
- **Testis:** testosterone

HPG



Control of male sexual functions by HPG:

GnRH :

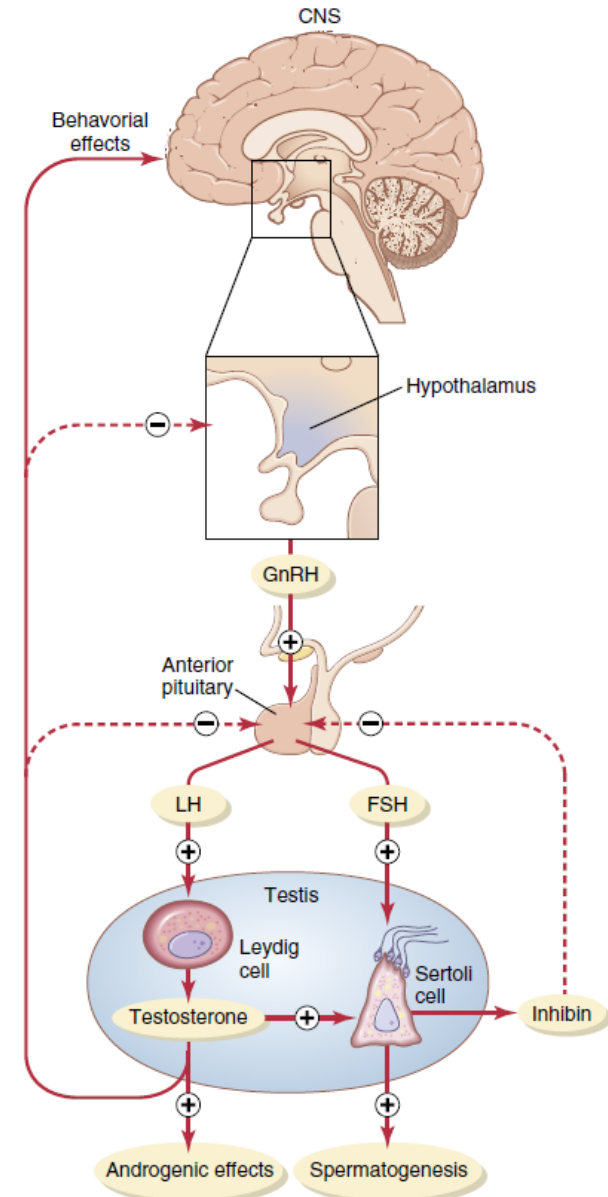
- A peptide secreted by the arcuate nuclei of the hypothalamus
- Released in the median eminence
- Carried via the hypothalamic-hypophysial portal blood vessels to the anterior pituitary.
- Stimulate anterior pituitary gland to release gonadotropins (LH and FSH).
- GnRH is secreted intermittently for few minutes every 1 to 3 hrs.
- Secretion of LH by the anterior pituitary is also cyclical following the **pulsatile** release of GnRH.

Regulation of Testosterone production by LH

- Testosterone is secreted by leydig cells, in the interstitium of the testis, by LH stimulation from the AP and
- Its release is directly proportional to the amount of LH.

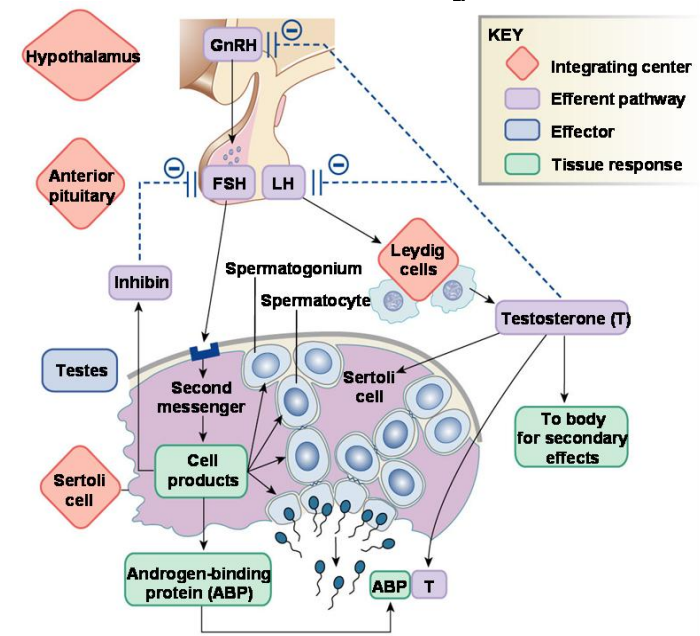
Negative feedback control of testosterone

- LH stimulate Testosterone secretion by the testis
- Testosterone inhibit the secretion of LH.
- Most of the inhibitory effect result from direct inhibition of GnRH release from the hypothalamus
- Inhibition of GnRH leads to decrease secretion of both LH & FSH.



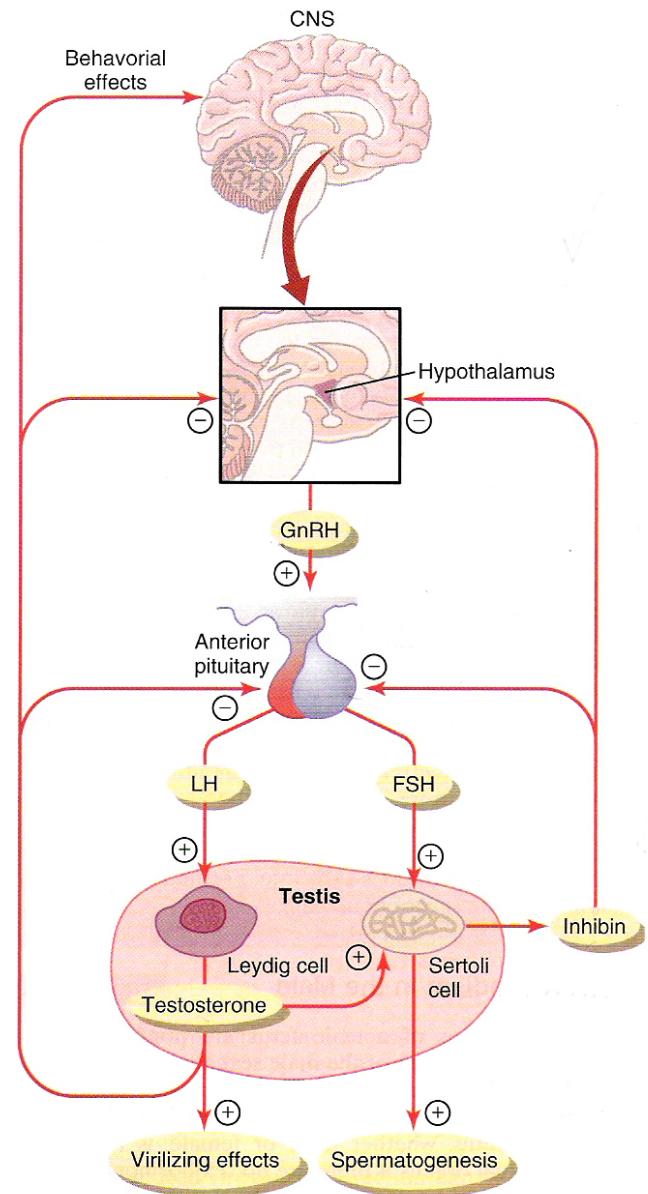
Regulation of spermatogenesis by FSH and testosterone

- **FSH** binds with specific FSH receptors on Sertoli cell in the seminiferous tubules, which causes these cells to grow & secrete spermatogenic substances.
- Testosterone & dihydrotestosterone diffuse into the seminiferous tubules from Leydig cells which affect spermatogenesis.
- Therefore, both FSH & testosterone are necessary to initiate spermatogenesis.



Negative feedback control of seminiferous tubule activity: Role of inhibin:

- When the seminiferous tubules fail to produce sperm, the secretion of **FSH** from the AP increases.
- Conversely, when spermatogenesis proceeds rapidly pituitary secretion of FSH diminishes.
- This is due to the secretion of inhibin hormone from the sertoli cells which strongly inhibit the AP- FSH
- Inhibin has slight inhibitory effect on the hypothalamus to inhibit GnRH secretion.

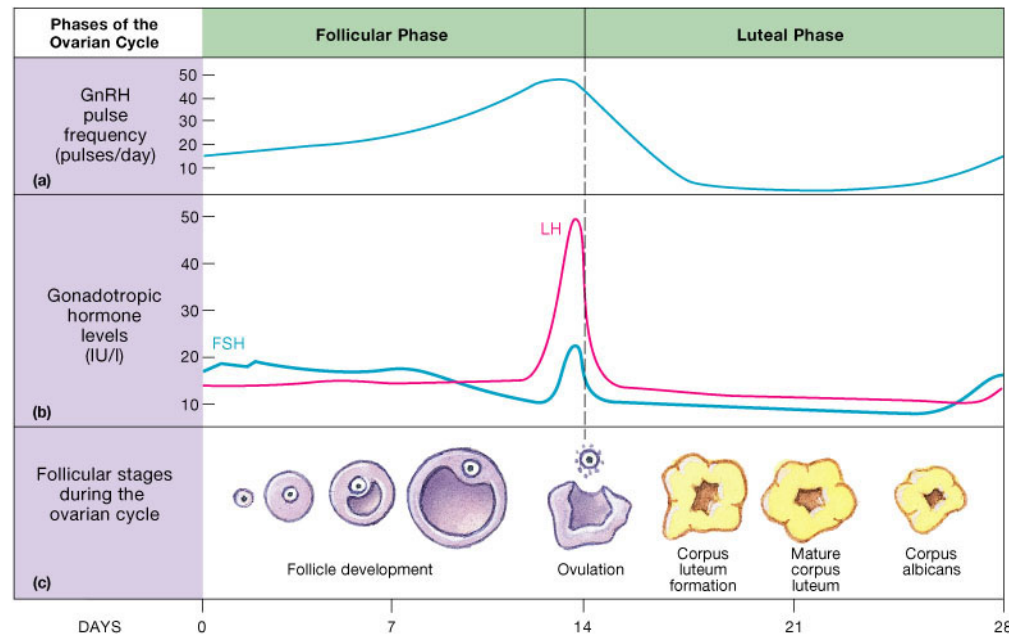


Regulation of the Female Monthly Rhythm: Interplay between the ovarian and hypothalamic-pituitary hormones:

- The neural activity that causes release of GnRH occurs in the arcuate nuclei which regulate most of the female sexual activity.
- GnRH is secreted in pulses lasting 5-25 minutes every 1-2 hrs.
- The pulsatile release of GnRH cause intermittent output of LH secretion about every 90 minutes.

Follicular phase

- After menstruation the level of FSH & LH increases
- Mainly FSH accelerates growth of few follicles (6-12 follicles).
- The growing follicle secretes increasing amounts of estrogen



Negative feedback effects of estrogen and progesterone

- Estrogen in small amounts has strong effect to inhibit the production of LH & FSH.
- This inhibitory effect of estrogen is increased when progesterone is available.
- This inhibitory effects more on the AP directly & to lesser extent on the hypothalamus to inhibit the secretion of GnRH.

Inhibin from the corpus luteum inhibits FSH secretion:

- The hormone inhibin secreted by the granulosa cells of the ovarian corpus luteum inhibit the secretion of FSH & to lesser extent LH.

Before Ovulation:

Positive feedback effect of estrogen before ovulation – the pre-ovulatory LH surge:

- AP secretes increased amount of LH for 1-2 days before ovulation.
- FSH surge is much smaller in the pre-ovulatory than LH surge.

The possible causes of LH secretion could be:

- Estrogen has special **positive feedback** effect of stimulating pituitary secretion of LH & to a lesser extent FSH
- The granulosa cells of the follicle begin to secrete small increasing amount of progesterone about 1 day before ovulation which stimulate LH secretion

After Ovulation:

Negative feedback:

- During the postovulatory phase the corpus luteum secrete large quantities of progesterone, estrogen & inhibin
- Which all together cause negative feedback effect on AP & hypothalamus to inhibit both FSH & LH secretion.

(lowest level 3-4 days before the onset of menstruation)

Follicular growth phase

- 2 -3 days before menstruation, corpus luteum regress & secretion of estrogen, progesterone & inhibin decrease.
- This decrease remove the negative feedback effect on AP hormones.
- Therefore a day after menstruation FSH secretion begins to increase (2 folds) while LH secretion is low.
- These hormones causes growth of a new follicle.
- During the first 11 to 12 days of the follicular growth the rate of secretion of FSH & LH decrease due to the negative feedback effect of estrogen on the AP.